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| EXAMINER | |
|---|---|
| LE, EMILY M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/733,489 | ILAN ET AL. | |
| | Examiner | Art Unit | |
| | Emily Le | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12/10/03+08/02/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-11,21 and 25-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-20 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/19/03+06/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group II and HCV viral infection, in the reply filed on 08/02/2005 is acknowledged.

Applicant traversed the restriction requirement by asserting that a search for the subject matter of Groups I-V does not constitute as a serious burden for the Examiner because the groups are related in their use of metabolites for treating diseases.

Applicant's submission has been considered, however, it is not found persuasive. In the instant, the invention of Group I is directed at the administration of an **intermediary metabolite** to treat a disease, the invention of Group II is directed at the use of a **reagent** to treat a disease, and the invention of Group V is directed at the use of a mammalian **metabolite** to treat a disease. While it is recognized that each of these inventions is directed at a method of treating a disease, however, the inventions are distinct from one another based on the material that is used in each of the inventions. The invention of Group I employs the administration of an intermediary metabolite. The invention of Group II employs the administration of a reagent, and the invention of Group V employs the administration of a mammalian metabolite. Each of these compositions is structurally different and has different functions.

Additionally, a search for a reagent that treats a disease does not equate to a search for a mammalian metabolite that treats a disease or an intermediary metabolite that treats a disease. In the instant, each of the listed inventions requires different fields of search. The search for the invention of Group I includes an intermediary metabolite,

whereas the search for the invention of Group II and III would include the terms reagent and mammalian metabolite. And a search for all terms would necessarily impose serious burden on the Office.

Furthermore, the inventions of Groups III-IV are distinct from the inventions of Groups I-II and V because these inventions have different modes of operation. The inventions of Groups III-IV are directed to processes that include active method steps that are different from those recited in the inventions of Groups I-II and V. The inventions of Groups III-IV are directed at the ex vivo treatment of a disease; whereas, the inventions of Groups I-II and V are directed at *in vivo* treatment techniques. These two techniques have separate status in the art, as evidenced by the different class and subclass assigned to the corresponding sets of groups.

In response to the restriction requirement set forth in the previous office action, Applicant further traversed the restriction requirement among cancer, infection and immune dysfunction. Applicant argues that the subject matter of the Groups focuses on administering a metabolite and a search for the use of a metabolite will encompass several diseases including by not limited to cancer, infection (viral and bacterial), and immune dysfunction.

Applicant's submission has been considered, however, it is not found persuasive. In the instant, a search for a population that is infected with a cancer would not overlap with a population infected with a bacteria or virus. Each of these different diseases is directed to a specific population of subjects. And a search for a population having a

bacterial infection does not necessarily overlap with a population having a viral infection. A search for all populations would impose a serious burden on the Office.

Additionally, Applicant asserts that a restriction requirement among HBV, HCV and HIV is inappropriate because the viruses share a common structure and function in accordance to *In re Harnish*.

Applicant's submission has been considered, however, it is not found persuasive. Contrary to Applicant's submission, HBV, HCV and HIV do not share a common structure. HBV, HCV and HIV do not even belong to the same family of viruses.

HBV is a member of the *Hepadnavirus* family. It consists of a proteinaceous core particle containing the viral genome in the form of double stranded DNA with single-stranded regions and an outer lipid-based envelope with embedded proteins.

HCV is a positive, single-stranded RNA virus in the *Flaviviridae* family. The genome is approximately 10,000 nucleotides and encodes a single polyprotein of about 3,000 amino acids.

And HIV is a member of the genus *lentivirus*, part of the family of retroviridae. In the instant, the viruses do not have significant structural similarity as Applicant asserted. Thus, Applicant's submission is not found persuasive. Therefore, because of the reason(s) set forth above, the requirement is still deemed proper and is therefore made **FINAL**.

***Status of Claims***

2. Claims 1-62 are pending. Claims 1-11, 21 and 25-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention,

there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/02/2005. Claims 12-20 and 22-24 are under examination.

***Information Disclosure Statement***

3. The information disclosure statement filed 06/24/2004 has been considered in full. The information disclosure statement filed 12/19/2003 has been considered in part. The documents listed under the U.S. Patent Documents are not considered, because the document numbers listed therein do not correspond to any U.S. Patent document.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

***Priority***

4. It is noted that this application appears to claim subject matter disclosed in prior Application No. 10/375906, filed 02/27/2003. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C.

111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 12-20 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed at the use of reagents to treat mammalian diseases.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly

allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under Vas- Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). **Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural**

**chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention**. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). See MPEP § 2163 for examination guidelines pertaining to the written description requirement.

In the instant, the specification does not teach of a single reagent that is useful in treating mammalian diseases. The drawings do not teach of a single reagent that is useful in treating mammalian diseases. Nor do the specification and the drawings provide any guidance pertaining to the biological activity of the reagent used with the claimed invention. The specification and drawings do not provide any guidance pertaining to the structural characteristics of the reagent used with the claimed invention.

The specification merely discussed Applicant's desire or contemplation of having a reagent that would increase the intracellular level of an intermediary metabolite, which would lead to an increase in the level of the corresponding metabolite, which would then modulate the immune system to treat mammalian diseases. [Paragraphs set forth on pages 4-5 of the specification] However, the specification is not specific as to what kind or type of reagent to use to treat mammalian diseases. The specification is not specific

as to the kind or type of intermediary metabolite to modulate by the reagent to treat mammalian diseases. The specification does not even set forth the kind and type of modulation necessary to treat mammalian diseases.

**Nothing exists in the specification, including the drawings, to suggest or demonstrate that a reagent useful in treating diseases was ever in Applicant's possession at the time of filing**. In the absence of any evidence suggesting or demonstrating that a reagent capable of treating diseases was ever in Applicant's possession, the claims are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

7. Claims 12-20 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

*Nature of the invention:*

The nature of the invention is directed at treating diseases with the administration of a reagent that would modulate the intermediary metabolite level, which would then modulate its corresponding metabolite level, wherein the modulation in the metabolite level treats mammalian diseases.

*Breadth of the claims:*

The broadest independent claim is directed at a process of treating mammalian diseases with the administration of a reagent that increases the level of an intermediary metabolite.

The breadth of the claims encompasses all diseases, all mammalian subjects, all reagents and all intermediary metabolites.

*Presence or absence of working examples:*

The specification does not contain any working examples directed at the administration of a reagent to treat mammalian diseases, including HCV.

All that is noted in the specification is an association between the Gaucher's disease and Hepatitis C virus infection. In the specification, Applicant notes that subjects diagnosed with Gaucher's disease and HCV infection have an immune profile

that is different from those diagnosed with only Gaucher's disease, all of which is summarized in Figures 1-6 in the specification.

Specifically, Applicant notes that: i) HCV specific T cell proliferation and the percent of peripheral natural killer T lymphocytes are less in subjects diagnosed with both Gaucher's disease and HCV infection compared to those diagnosed with only Gaucher's disease; and ii) the level of interferon gamma, interleukin-10, interleukin-4 observed in subjects diagnosed with both Gaucher's disease and HCV are higher than those diagnosed with only Gaucher's disease.

*Amount of direction or guidance presented:*

Beside the weak association between various immunoparameters in subjects diagnosed with only Gaucher's disease and those diagnosed with both HCV and Gaucher's disease, the specification does not provide any additional guidance pertaining to the relevance of the observations made via the working examples.

The specification does not set forth any guidance that would bridge the gap between the observations made by Applicant in the specification and the claimed invention. The specification does not provide any guidance directing at the type or kind of reagent that the skilled artisan should use to treat mammalian diseases. The specification does not even contain any guidance relating to the structural characteristics of reagents used with the claimed invention. There is not even a teaching of the intermediary metabolite that the reagent should modulate to treat mammalian diseases. The specification does not even contain any guidance relating to the mammalian disease(s) that is treatable by modulation of the metabolite level.

In the instant, **the specification is fatally defective**.

*State of the prior art:*

At the time of filing of the instant patent application, the art recognizes that there are approximately 800 to 2000 different metabolites assayed in human subjects.[1] And a search of the literature renders that there are more than 4000 different diseases, as evidenced by the alphabetical listing of diseases compiled by Karolinska Institutet. Karolinska Institutet summarizes that the 4000 plus diseases fall into the following categories: Bacterial Infections and Mycoses, Virus Diseases, Parasitic Diseases, Neoplasms (Cancer), Musculoskeletal Diseases, Digestive System Diseases, Stomatognathic Diseases, Respiratory Tract Diseases, Otorhinolaryngologic Diseases, Nervous System Diseases, Eye Diseases, Urologic and Male Genital Diseases, Female Genital Diseases and Pregnancy Complications, Cardiovascular Diseases, Hemic and Lymphatic Diseases, Congenital, Hereditary, and Neonatal Diseases and Abnormalities, Skin and Connective Tissue Diseases, Nutritional and Metabolic Diseases, Endocrine Diseases, Immunologic Diseases, Disorders of Environmental Origin/Poisoning, Animal Diseases, Pathological Conditions, Signs and Symptoms, Behavior and Behavior Mechanisms, and Mental Disorders. (A listing of diseases is attached. The complete listing of diseases is retrieved from http://www.mic.ki.se/Diseases/Alphalist.html.)

*Quantity of experimentation necessary:*

The skilled artisan cannot rely on the disclosure set forth in the specification to reasonably practice the invention without an undue burden of experimentation. In order

for the skilled artisan to successfully practice the claimed invention, the skilled artisan would have to unduly and blindly experiment with each known diseases, metabolites and reagents to establish a relevance each of the listed variables has over the other. The skilled artisan would need to establish a relationship between each known metabolites with each known diseases. From this establishment, the skilled artisan would have to determine if the metabolite would is useful in treating the disease or diseases. Then, the skilled artisan would have to determine if the metabolite is capable of treating disease or diseases. Following the determination, the skilled artisan would then have to correlate the metabolite with the reagent. In correlating the metabolite with the reagent, the skilled artisan must demonstrate that the reagent is capable of modulating the metabolite in the manner necessary to treat diseases.

In all, the skilled artisan would have to bridge the gap among the use of a reagent to increase metabolites and treatment of mammalian diseases. In the instant, the attainment of such knowledge would undeniably be an undoubtedly laborious task that includes both undue and blind experimentations. Compound to the quantity of experimentations required of the skilled artisan is the large abundance of information to mine and analyze, as demonstrated by the number of diseases and metabolites known in the art. In the instant, quantity of experimentation that the skilled artisan would have to conduct is endless. And the imposition of endless experiments would unarguably be an undue burden for the skilled artisan.

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[1] Beecher W.C., Metabolic Profiling: Its Role in Biomarker Discovery and Gene Function Analysis, Chapter 17: The human metabolome. *Kluwer Academic, 2003.*

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

***Conclusion***

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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